Agency for Healthcare Research and Quality
Advancing Excellence in Health Care

NATIONAL GUIDELINE CLEARINGHOUSE

General

Guideline Title

Antiemetics: American Society of Clinical Oncology clinical practice guideline update.

Bibliographic Source(s)

Hesketh PJ, Kris MG, Basch E, Bohlke K, Barbour SY, Clark-Snow RA, Danso MA, Dennis K, Dupuis LL, Dusetzina SB, Eng C, Feyer PC, Jordan K, Noonan K, Sparacio D, Somerfield MR, Lyman GH. Antiemetics: American Society of Clinical Oncology clinical practice guideline update. J Clin Oncol. 2017 Oct 1;35(28):3240-61. [121 references] PubMed

Guideline Status

This is the current release of the guideline.

This guideline updates a previous version: Basch E, Prestrud AA, Hesketh PJ, Kris MG, Feyer PC, Somerfield MR, Chesney M, Clark-Snow RA, Flaherty AM, Freundlich B, Morrow G, Rao KV, Schwartz RN, Lyman GH. Antiemetics: American Society of Clinical Oncology clinical practice guideline update. J Clin Oncol. 2011 Nov 1;29(31):4189-98. [56 references]

This guideline meets NGC's 2013 (revised) inclusion criteria.

NEATS Assessment

National Guideline Clearinghouse (NGC) has assessed this guideline's adherence to standards of trustworthiness, derived from the Institute of Medicine's report Clinical Practice Guidelines We Can Trust.

= Poor = Fair = Good = Very Good = Excellent

Assessment	Standard of Trustworthiness
YES	Disclosure of Guideline Funding Source
	Disclosure and Management of Financial Conflict of Interests

	Guideline Development Group Composition
YES	Multidisciplinary Group
YES	Methodologist Involvement
▮▮▮▮▯	Patient and Public Perspectives
	Use of a Systematic Review of Evidence
▮▮▮▮▮	Search Strategy
▮▮▮▮▮	Study Selection
▮▮▮▮▮	Synthesis of Evidence
	Evidence Foundations for and Rating Strength of Recommendations
▮▮▮▮▮	Grading the Quality or Strength of Evidence
▮▮▮▮▮	Benefits and Harms of Recommendations
▮▮▮▮▮	Evidence Summary Supporting Recommendations
▮▮▮▮▮	Rating the Strength of Recommendations
▮▮▮▮▮	Specific and Unambiguous Articulation of Recommendations
▮▮▮▮▯	External Review
▮▮▮▮▮	Updating

Recommendations

Major Recommendations

Definitions for the rating of evidence (High, Intermediate, Low, Insufficient); types of recommendations (Evidence based, Formal consensus, Informal consensus, No recommendation); and strength of recommendations (Strong, Moderate, Weak) are provided at the end of the "Major Recommendations" field.

Antineoplastic Agent-Induced Nausea and Vomiting in Adults

Tables 1 and 2 in the original guideline document list intravenous (IV) and oral antineoplastic agents by emetic risk. Adult antiemetic dosing schedules for each risk class are listed in Table 3 in the original guideline document.

Clinical Question 1. What is the optimal treatment to prevent nausea and vomiting as a result of high-emetic-risk antineoplastic agents in adults who receive single-day antineoplastic agent therapy?

Recommendation 1.1: Adult patients who are treated with cisplatin and other high-emetic-risk single agents should be offered a four-drug combination of a neurokinin 1 (NK_1) receptor antagonist, a serotonin (5-hydroxytryptamine-3 [$5\text{-}HT_3$]) receptor antagonist, dexamethasone, and olanzapine. Dexamethasone

and olanzapine should be continued on days 2 to 4 (Type: evidence based, benefits outweigh harms; Quality of evidence: high; Strength of recommendation: strong).

Recommendation 1.2: Adult patients who are treated with an anthracycline combined with cyclophosphamide (AC) should be offered a four-drug combination of an NK_1 receptor antagonist, a 5-HT_3 receptor antagonist, dexamethasone, and olanzapine. Olanzapine should be continued on days 2 to 4 (Type: evidence based, benefits outweigh harms; Quality of evidence: high; Strength of recommendation: strong).

Clinical Question 2. What is the optimal treatment to prevent nausea and vomiting from moderate-emetic-risk antineoplastic agents in adults who receive single-day antineoplastic agent therapy?

Recommendation 2.1: Adult patients who are treated with carboplatin area under the curve (AUC) ≥ 4 mg/mL per minute should be offered a three-drug combination of an NK_1 receptor antagonist, a 5-HT_3 receptor antagonist, and dexamethasone (Type: evidence based, benefits outweigh harms; Quality of evidence: high; Strength of recommendation: strong).

Recommendation 2.2: Adult patients who are treated with moderate-emetic-risk antineoplastic agents—excluding carboplatin AUC ≥ 4 mg/mL per minute—should be offered a two-drug combination of a 5-HT_3 receptor antagonist (day 1) and dexamethasone (day 1) (Type: evidence based, benefits outweigh harms; Quality of evidence: high; Strength of recommendation: strong).

Recommendation 2.3: Adult patients who are treated with cyclophosphamide, doxorubicin, oxaliplatin, and other moderate-emetic-risk antineoplastic agents that are known to cause delayed nausea and vomiting may be offered dexamethasone on days 2 to 3 (Type: informal consensus, benefits outweigh harms; Quality of evidence: low; Strength of recommendation: moderate).

Clinical Question 3. What is the optimal treatment to prevent nausea and vomiting from low-emetic-risk antineoplastic agents in adults who receive single-day antineoplastic agent therapy?

Recommendation 3: Adult patients who are treated with low-emetic-risk antineoplastic agents should be offered a single dose of a 5-HT_3 receptor antagonist or a single 8-mg dose of dexamethasone before antineoplastic treatment (Type: informal consensus, benefits outweigh harms; Quality of evidence: low; Strength of recommendation: moderate).

Clinical Question 4. What is the optimal treatment to prevent nausea and vomiting from minimal-emetic-risk antineoplastic agents in adults who receive single-day antineoplastic agent therapy?

Recommendation 4: Adult patients who are treated with minimal-emetic-risk antineoplastic agents should not be offered routine antiemetic prophylaxis (Type: informal consensus, benefits outweigh harms; Quality of evidence: low; Strength of recommendation: moderate).

Clinical Question 5. What is the optimal treatment to prevent nausea and vomiting in adults who receive single-day combination antineoplastic agent therapy?

Recommendation 5: Adult patients who are treated with antineoplastic combinations should be offered antiemetics that are appropriate for the component antineoplastic agent of greatest emetic risk (Type: informal consensus, benefits outweigh harms; Quality of evidence: intermediate; Strength of recommendation: moderate).

Clinical Question 6. What is the role of adjunctive drugs for nausea and vomiting after cancer treatments?

Recommendation 6: Lorazepam is a useful adjunct to antiemetic drugs but is not recommended as a single-agent antiemetic (Type: informal consensus; benefits outweigh harms; Quality of evidence: low; Strength of recommendation: moderate).

Clinical Question 7. What is the role of cannabinoids in the prevention or treatment of nausea and vomiting induced by antineoplastic agents or radiation?

Recommendation 7: Evidence remains insufficient for a recommendation regarding medical marijuana for the prevention of nausea and vomiting in patients with cancer who receive chemotherapy or radiation therapy. Evidence is also insufficient for a recommendation regarding the use of medical marijuana in place of the tested and U.S. Food and Drug Administration–approved cannabinoids, dronabinol and nabilone, for the treatment of nausea and vomiting caused by chemotherapy or radiation therapy.

Clinical Question 8. What is the role of complementary and alternative therapies in the prevention or treatment of nausea and vomiting induced by antineoplastic agents or radiation?

Recommendation 8: Evidence remains insufficient for a recommendation for or against the use of ginger, acupuncture/acupressure, and other complementary or alternative therapies for the prevention of nausea and vomiting in patients with cancer.

Clinical Question 9. What is the optimal treatment for the prevention of nausea and vomiting in patients who are undergoing high-dose chemotherapy for stem cell or bone marrow transplantation conditioning?

Recommendation 9: Adult patients who are treated with high-dose chemotherapy and stem cell or bone marrow transplantation should be offered a three-drug combination of an NK_1 receptor antagonist, 5-HT_3 receptor antagonist, and dexamethasone (Type: evidence based, benefits outweigh harms; Quality of evidence: high; Strength of recommendation: strong).

Clinical Question 10. What is the optimal treatment for the prevention of nausea and vomiting for adults who receive multiday antineoplastic agent therapy?

Recommendation 10.1: Adult patients who are treated with multiday antineoplastic agents should be offered antiemetics before treatment that are appropriate for the emetic risk of the antineoplastic agent administered on each day of the antineoplastic treatment and for 2 days after completion of the antineoplastic regimen (Type: evidence based, benefits outweigh harms; Quality of evidence: intermediate; Strength of recommendation: moderate).

Recommendation 10.2: Adult patients who are treated with 4- or 5-day cisplatin regimens should be offered a three-drug combination of an NK_1 receptor antagonist, a 5-HT_3 receptor antagonist, and dexamethasone (Type: evidence based, benefits outweigh harms; Quality of evidence: high; Strength of recommendation: strong).

Clinical Question 11. What is the optimal antiemetic regimen for adults who experience nausea and vomiting secondary to therapy with an antineoplastic agent despite optimal prophylaxis (breakthrough)?

Recommendation 11.1: For patients with breakthrough nausea or vomiting, clinicians should re-evaluate emetic risk, disease status, concurrent illnesses, and medications and ascertain that the best regimen is being administered for the emetic risk (Type: informal consensus, benefits outweigh harms; Quality of evidence: low; Strength of recommendation: moderate).

Recommendation 11.2: Adult patients who experience nausea or vomiting despite optimal prophylaxis, and who did not receive olanzapine prophylactically, should be offered olanzapine in addition to continuing the standard antiemetic regimen (Type: evidence based, benefits outweigh harms; Quality of evidence: intermediate; Strength of recommendation: moderate).

Recommendation 11.3: Adult patients who experience nausea or vomiting despite optimal prophylaxis, and who have already received olanzapine, may be offered a drug of a different class—for example, an NK_1 receptor antagonist, lorazepam or alprazolam, a dopamine receptor antagonist, dronabinol, or nabilone—in addition to continuing the standard antiemetic regimen (Type: informal consensus, benefits outweigh harms; Quality of evidence: intermediate for dronabinol and nabilone, low otherwise; Strength of recommendation: moderate).

Clinical Question 12. What treatment options are available for adults who experience anticipatory nausea and vomiting?

Recommendation 12: All patients should receive the most active antiemetic regimen appropriate for the antineoplastic agents being administered. Clinicians should use such regimens with initial antineoplastic treatment, rather than assessing the patient's emetic response with less effective antiemetic treatment. If a patient experiences anticipatory emesis, clinicians may offer behavioral therapy with systematic desensitization (Type: informal consensus, benefits outweigh harms; Quality of evidence: low; Strength of recommendation: moderate).

Radiation-Induced Nausea and Vomiting in Adults

Updated risk stratification according to site of radiation treatment is provided in Table 4 in the original guideline document. Dosing schedules according to risk are listed in Table 5 in the original guideline document.

Clinical Question 13. What is the optimal prophylaxis for nausea and vomiting caused by high-emetic-risk radiation?

Recommendation 13: Adult patients who are treated with high-emetic-risk radiation therapy should be offered a two-drug combination of a 5-HT_3 receptor antagonist and dexamethasone before each fraction and on the day after each fraction if radiation therapy is not planned for that day (Type: evidence based, benefits outweigh harms; Quality of evidence: high; Strength of recommendation: strong).

Clinical Question 14. What is the optimal prophylaxis for nausea and vomiting caused by moderate-emetic-risk radiation therapy?

Recommendation 14: Adult patients who are treated with moderate-emetic-risk radiation therapy should be offered a 5-HT_3 receptor antagonist before each fraction, with or without dexamethasone before the first five fractions (Type: evidence based, benefits outweigh harms; Quality of evidence: high; Strength of recommendation: moderate).

Clinical Question 15. What is the optimal treatment to manage nausea and vomiting associated with low-emetic-risk radiation therapy?

Recommendation 15: Adult patients who are treated with radiation therapy to the brain should be offered rescue dexamethasone therapy. Adult patients who are treated with radiation therapy to the head and neck, thorax, or pelvis should be offered rescue therapy with a 5-HT_3 receptor antagonist, dexamethasone, or a dopamine receptor antagonist (Type: informal consensus, benefits outweigh harms; Quality of evidence: low; Strength of recommendation: weak).

Clinical Question 16. What is the optimal treatment to manage nausea and vomiting associated with minimal-emetic-risk radiation therapy?

Recommendation 16: Adult patients who are treated with minimal-emetic-risk radiation therapy should be offered rescue therapy with a 5-HT_3 receptor antagonist, dexamethasone, or a dopamine receptor antagonist (Type: informal consensus, benefits outweigh harms; Quality of evidence: low; Strength of recommendation: weak).

Clinical Question 17. What is the optimal treatment for the management of nausea and vomiting during concurrent radiation and antineoplastic agent therapy?

Recommendation 17: Adult patients who are treated with concurrent radiation and antineoplastic agents should receive antiemetic therapy that is appropriate for the emetic risk level of the antineoplastic agents, unless the risk level of the radiation therapy is higher. During periods when prophylactic antiemetic therapy for the antineoplastic agents has ended and ongoing radiation therapy would normally be managed with its own prophylactic therapy, patients should receive prophylactic therapy that is appropriate for the emetic risk of the radiation therapy until the next period of antineoplastic therapy, rather than receiving rescue therapy for the antineoplastic agents as needed (Type: informal consensus, benefits outweigh harms; Quality of evidence: intermediate; Strength of recommendation: moderate).

Antineoplastic Agent-Induced Nausea and Vomiting in Pediatric Patients

Pediatric clinicians should consult recognized pediatric drug formularies for information regarding appropriate pediatric dosing of antiemetic agents.

Clinical Question 18. What is the optimal treatment to prevent nausea and vomiting from high-emetic-risk antineoplastic agents in pediatric patients?

Recommendation 18.1: Pediatric patients who are treated with high-emetic-risk antineoplastic agents should be offered a three-drug combination of a 5-HT_3 receptor antagonist, dexamethasone, and aprepitant (Type: evidence based, benefits outweigh harms; Quality of evidence: intermediate; Strength of recommendation: strong).

Recommendation 18.2: Pediatric patients who are treated with high-emetic-risk antineoplastic agents who are unable to receive aprepitant should be offered a two-drug combination of a 5-HT_3 receptor antagonist and dexamethasone (Type: evidence based, benefits outweigh harms; Quality of evidence: intermediate; Strength of recommendation: strong).

Recommendation 18.3: Pediatric patients who are treated with high-emetic-risk antineoplastic agents who are unable to receive dexamethasone should be offered a two-drug combination of palonosetron and aprepitant (Type: evidence based, benefits outweigh harms; Quality of evidence: intermediate; Strength of recommendation: strong).

Clinical Question 19. What is the optimal treatment to prevent nausea and vomiting from moderate-emetic-risk antineoplastic agents in pediatric patients?

Recommendation 19.1: Pediatric patients who are treated with moderate-emetic-risk antineoplastic agents should be offered a two-drug combination of a 5-HT_3 receptor antagonist and dexamethasone (Type: evidence based, benefits outweigh harms; Quality of evidence: intermediate; Strength of recommendation: strong).

Recommendation 19.2: Pediatric patients who are treated with moderate-emetic-risk antineoplastic agents and who are unable to receive dexamethasone should be offered a two-drug combination of a 5-HT_3 receptor antagonist and aprepitant (Type: evidence based, benefits outweigh harms; Quality of evidence: intermediate; Strength of recommendation: weak).

Clinical Question 20. What is the optimal treatment to prevent nausea and vomiting from low-emetic-risk antineoplastic agents in pediatric patients?

Recommendation 20: Pediatric patients who are treated with low-emetic-risk antineoplastic agents should be offered ondansetron or granisetron (Type: informal consensus, benefits outweigh harms; Quality of evidence: low; Strength of recommendation: strong).

Clinical Question 21. What is the optimal treatment to prevent nausea and vomiting from minimal-emetic-risk antineoplastic agents in pediatric patients?

Recommendation 21: Pediatric patients who are treated with minimal-emetic-risk antineoplastic agents should not be offered routine antiemetic prophylaxis (Type: informal consensus, benefits outweigh harms; Quality of evidence: low; Strength of recommendation: strong).

New Agents and Formulations

New antiemetic medications that have become available since the previous update are rolapitant—an NK_1 receptor antagonist—and granisetron—a 5-HT_3 receptor antagonist—extended-release injection. The dosing of these agents is provided in Table 3 in the original guideline document.

Definitions

Guide for Rating Quality of Evidence

Rating for Strength of Evidence	Definition
High	High confidence that the available evidence reflects the true magnitude and direction of the net effect (i.e., balance of benefits versus harms) and that further research is very unlikely to change either the magnitude or direction of this net effect.
Intermediate	Moderate confidence that the available evidence reflects the true magnitude and direction of the net effect. Further research is unlikely to alter the direction of the net effect; however, it might alter the magnitude of the net effect.
Low	Low confidence that the available evidence reflects the true magnitude and direction of the net effect. Further research may change either the magnitude and/or direction this net effect.
Insufficient	Evidence is insufficient to discern the true magnitude and direction of the net effect. Further research may better inform the topic. The use of the consensus opinion of experts is reasonable to inform outcomes related to the topic.

Guide for Types of Recommendations

Type of Recommendation	Definition
Evidence based	There was sufficient evidence from published studies to inform a recommendation to guide clinical practice.
Formal consensus	The available evidence was deemed insufficient to inform a recommendation to guide clinical practice. Therefore, the Expert Panel used a formal consensus process to reach this recommendation, which is considered the best current guidance for practice. The Expert Panel may choose to provide a rating for the strength of the recommendation (i.e., "strong," "moderate," or "weak"). The results of the formal consensus process are summarized in the guideline and reported in the Data Supplement (see the "Availability of Companion Documents" field).
Informal Consensus	The available evidence was deemed insufficient to inform a recommendation to guide clinical practice. The recommendation is considered the best current guidance for practice, based on informal consensus of the Expert Panel. The Expert Panel agreed that a formal consensus process was not necessary for reasons described in the literature review and discussion. The Expert Panel may choose to provide a rating for the strength of the recommendation (i.e., "strong," "moderate," or "weak").
No recommendation	There is insufficient evidence, confidence, or agreement to provide a recommendation to guide clinical practice at this time. The Expert Panel deemed the available evidence as insufficient and concluded it was unlikely that a formal consensus process would achieve the level of agreement needed for a recommendation.

Guide for Strength of Recommendations

Rating for Strength of Recommendation	Definition
Strong	There is high confidence that the recommendation reflects best practice. This is based on (1) strong evidence for a true net effect (e.g., benefits exceed harms); (2) consistent results, with no or minor exceptions; (3) minor or no concerns about study quality; and/or (4) the extent of Expert Panelists' agreement. Other compelling considerations (discussed in the guideline's literature review and analyses) may also warrant a strong recommendation.
Moderate	There is moderate confidence that the recommendation reflects best practice. This is based on (1) good evidence for a true net effect (e.g., benefits exceed harms); (2) consistent results, with minor and/or few exceptions; (3) minor and/or few concerns about study quality; and/or (4) the extent of Expert Panelists' agreement. Other compelling considerations (discussed in the guideline's literature review and analyses) may also warrant a moderate recommendation.

Rating for Strength of Recommendation	Definition
Weak	There is some confidence that the recommendation offers the best current guidance for practice. This is based on (1) limited evidence for a true net effect (e.g., benefits exceed harms); (2) consistent results, but with important exceptions; (3) concerns about study quality; and/or (4) the extent of Expert Panelists' agreement. Other considerations (discussed in the guideline's literature review and analyses) may also warrant a weak recommendation.

Clinical Algorithm(s)

None provided

Scope

Disease/Condition(s)

Nausea and vomiting due to antineoplastic agents or radiation therapy

Guideline Category

Assessment of Therapeutic Effectiveness

Management

Prevention

Risk Assessment

Treatment

Clinical Specialty

Oncology

Pediatrics

Pharmacology

Radiation Oncology

Intended Users

Advanced Practice Nurses

Nurses

Patients

Pharmacists

Physician Assistants

Physicians

Guideline Objective(s)

To provide updated recommendations to prevent and manage nausea and vomiting caused by antineoplastic agents or radiation therapy for cancer

Target Population

Adults and children who receive antineoplastic agents and adults who undergo radiation therapy for cancer

Interventions and Practices Considered

1. Antiemetic pharmacotherapy based on emetic risk and type of cancer treatment
    - Neurokinin 1 (NK_1) receptor antagonists (aprepitant)
    - Serotonin 5-hydroxytryptamine-3 ($5\text{-}HT_3$) receptor antagonists (granisetron, ondansetron, palonosetron)
    - Dexamethasone
    - Olanzapine
    - Dopamine receptor antagonists
    - Combination treatments
2. Adjunctive drugs (lorazepam, alprazolam
3. Cannabinoids (dronabinol, nabilone)
4. Behavioral therapy with systematic desensitization
5. Re-evaluation of patients with breakthrough nausea and vomiting

Note: The following were considered but not recommended: routine antiemetic prophylaxis in adult or pediatric patients treated with minimal-emetic-risk antineoplastic agents and lorazepam as a single-agent antiemetic. No recommendation for or against can be made due to insufficient evidence for the following: medical marijuana, ginger, acupuncture/acupressure, other complementary or alternative therapies.

Major Outcomes Considered

- Complete response
- Emetic episodes
- Nausea control
- Use of rescue medication
- Adverse effects of medications

Methodology

Methods Used to Collect/Select the Evidence

Hand-searches of Published Literature (Primary Sources)

Hand-searches of Published Literature (Secondary Sources)

Searches of Electronic Databases

Description of Methods Used to Collect/Select the Evidence

Systematic Literature Review

The American Society of Clinical Oncology (ASCO) guidelines are based on systematic reviews of the literature. A protocol for each systematic review defines parameters for a targeted literature search.

Additional parameters include relevant study designs, literature sources, types of reports, and pre-specified inclusion and exclusion criteria for literature identified.

PubMed and the Cochrane Library were searched from November 1, 2009, to June 1, 2016. The updated search was restricted to articles that were published in English and to randomized controlled trials (RCTs) and meta-analyses of RCTs. Search terms are listed in the Data Supplement (see the "Availability of Companion Documents" field). RCTs were required to have at least 25 patients per arm and at least 5 days—120 hours—of follow-up. The updated search was guided by the signals approach that is designed to identify only new, potentially practice-changing data—signals—that might translate into revised practice recommendations. This approach relies on targeted routine literature searching and the expertise of ASCO Expert Panel members to help identify potential signals. The Methodology Supplement (see the "Availability of Companion Documents" field) provides additional information on the signals approach.

As in the 2011 ASCO guideline, the emetic risk of antineoplastic mediations was classified by using four levels based on the likelihood of emesis in the absence of antiemetic prophylaxis: high (>90%), moderate (30% to 90%), low (10% to 30%), and minimal (<10%). The 2011 ASCO guideline only addressed the emetic risk of intravenous (IV) antineoplastic agents. To update that list as well as to add information about the emetic risk of oral antineoplastic agents, the Expert Panel incorporated information from a 2016 publication by the Multinational Association of Supportive Care in Cancer (MASCC) and the European Society of Medical Oncology (ESMO). The Expert Panel also updated the MASCC/ESMO search to identify drugs that had been approved since their review. For these additional drugs, the Expert Panel collected information and classified emetic risk according to methods developed by MASCC/ESMO.

Radiation treatments were also classified as posing a high, moderate, low, or minimal risk of inducing nausea and vomiting, depending on the anatomic region being irradiated. No other patient-, tumor-, or treatment-related factors presently inform this classification. The incidence of radiation-induced nausea and vomiting after radiation therapy to many anatomic regions remains unclear as a result of heterogeneity among study patient populations, designs, outcome measures, total doses, doses per fraction, doses administered to individual organs, target volumes, and radiation therapy techniques. The Expert Panel supports the four-level risk classification for radiation-induced nausea and vomiting but notes that evidence for radiation-induced nausea and vomiting and its relationship to discrete irradiated anatomic regions is limited, especially for low- and minimal-emetic-risk radiation therapy. In addition, most of the evidence for radiation-induced nausea and vomiting was collected before the widespread implementation of highly conformal radiation therapy techniques that likely modulate the risk of radiation-induced nausea and vomiting.

Number of Source Documents

A total of 41 publications were included in the systematic review: 35 randomized controlled trials (RCTs) and six meta-analyses. Emetic risk information for 19 new antineoplastic agents was abstracted from a total of 36 clinical trials.

See Data Supplement 4 (see the "Availability of Companion Documents" field) for a Quality of Reporting of Meta-analyses (QUOROM) Diagram showing exclusions and inclusions of publications identified for the systematic review.

Methods Used to Assess the Quality and Strength of the Evidence

Weighting According to a Rating Scheme (Scheme Given)

Rating Scheme for the Strength of the Evidence

Guide for Rating Quality of Evidence

Rating for Strength of Evidence	Definition
High	High confidence that the available evidence reflects the true magnitude and direction of the net effect (i.e., balance of benefits versus harms) and that further research is very unlikely to change either the magnitude or direction of this net effect.
Intermediate	Moderate confidence that the available evidence reflects the true magnitude and direction of the net effect. Further research is unlikely to alter the direction of the net effect; however, it might alter the magnitude of the net effect.
Low	Low confidence that the available evidence reflects the true magnitude and direction of the net effect. Further research may change either the magnitude and/or direction this net effect.
Insufficient	Evidence is insufficient to discern the true magnitude and direction of the net effect. Further research may better inform the topic. The use of the consensus opinion of experts is reasonable to inform outcomes related to the topic.

Guide for Rating of Potential for Bias

Rating of Potential for Bias	Definitions for Rating Potential for Risk of Bias in Randomized Controlled Trials
Low risk	No major features in the study that risk biased results, and none of the limitations are thought to decrease the validity of the conclusions. The study avoids problems such as failure to apply true randomization, selection of a population unrepresentative of the target patients, high dropout rates, and no intention-to-treat analysis; and key study features are described clearly (including the population, setting, interventions, comparison groups, measurement of outcomes, and reasons for dropouts).
Intermediate	The study is susceptible to some bias, but flaws are not sufficient to invalidate the results. Enough of the items introduce some uncertainty about the validity of the conclusions. The study does not meet all the criteria required for a rating of good quality, but no flaw is likely to cause major bias. The study may be missing information, making it difficult to assess limitations and potential problems.
High risk	There are significant flaws that imply biases of various types that may invalidate the results. Several of the items introduce serious uncertainty about the validity of the conclusions. The study has serious errors in design, analysis, or reporting; large amounts of missing information; or discrepancies in reporting.

Methods Used to Analyze the Evidence

Review of Published Meta-Analyses

Systematic Review with Evidence Tables

Description of the Methods Used to Analyze the Evidence

Data Extraction

Literature search results were reviewed and deemed appropriate for full text review by one American Society of Clinical Oncology (ASCO) staff reviewer in consultation with the Expert Panel Co-Chairs. Data were extracted by one staff reviewer and subsequently checked for accuracy through an audit of the data by another ASCO staff member. Disagreements were resolved through discussion and consultation with the Co-Chairs if necessary. Evidence tables are provided in Data Supplements 1 and 2 (see the "Availability of Companion Documents" field).

Study Quality Assessment

Study quality was formally assessed for the studies identified. Design aspects related to the individual study quality were assessed by one reviewer and included factors such as blinding, allocation

concealment, placebo control, intention to treat, funding sources, etc. The risk of bias is assessed as "low," "intermediate," or "high" for most of the identified evidence (see the "Rating Scheme for the Strength of the Evidence" field).

Methods Used to Formulate the Recommendations

Expert Consensus

Informal Consensus

Description of Methods Used to Formulate the Recommendations

Guideline Update Development Process

The American Society of Clinical Oncology (ASCO) convened an Expert Panel to consider the evidence and formulate the recommendations. Members of the Expert Panel were drawn from both community and academic settings and have expertise in medical oncology, radiation oncology, nursing, pharmacy, and health services research. The panel also included a patient representative. The Expert Panel met via teleconference and in person and corresponded through e-mail. On the basis of a consideration of the evidence, the authors were asked to contribute to the development of the guideline, provide critical review, and finalize guideline recommendations. Recommendations developed by the Expert Panel are based on a systematic review of the medical literature and clinical experience.

Guideline recommendations were crafted, in part, by using the Guidelines Into Decision Support (GLIDES) methodology. In addition, a review of the ability to implement the guideline was conducted. Ratings for the type and strength of recommendation and the quality of the evidence are provided with each recommendation. In selected cases in which evidence was lacking—but there was a high level of agreement among Expert Panel members—informal consensus was used.

Rating Scheme for the Strength of the Recommendations

Guide for Types of Recommendations

Type of Recommendation	Definition
Evidence based	There was sufficient evidence from published studies to inform a recommendation to guide clinical practice.
Formal consensus	The available evidence was deemed insufficient to inform a recommendation to guide clinical practice. Therefore, the Expert Panel used a formal consensus process to reach this recommendation, which is considered the best current guidance for practice. The Expert Panel may choose to provide a rating for the strength of the recommendation (i.e., "strong," "moderate," or "weak"). The results of the formal consensus process are summarized in the guideline and reported in the Data Supplement (see the "Availability of Companion Documents" field).
Informal Consensus	The available evidence was deemed insufficient to inform a recommendation to guide clinical practice. The recommendation is considered the best current guidance for practice, based on informal consensus of the Expert Panel. The Expert Panel agreed that a formal consensus process was not necessary for reasons described in the literature review and discussion. The Expert Panel may choose to provide a rating for the strength of the recommendation (i.e., "strong," "moderate," or "weak").
No recommendation	There is insufficient evidence, confidence, or agreement to provide a recommendation to guide clinical practice at this time. The Expert Panel deemed the available evidence as insufficient and concluded it was unlikely that a formal consensus process would achieve the level of agreement needed for a recommendation.

Guide for Strength of Recommendations

Rating for Strength of Recommendation	Definition
Strong	There is high confidence that the recommendation reflects best practice. This is based on (1) strong evidence for a true net effect (e.g., benefits exceed harms); (2) consistent results, with no or minor exceptions; (3) minor or no concerns about study quality; and/or (4) the extent of Expert Panelists' agreement. Other compelling considerations (discussed in the guideline's literature review and analyses) may also warrant a strong recommendation.
Moderate	There is moderate confidence that the recommendation reflects best practice. This is based on (1) good evidence for a true net effect (e.g., benefits exceed harms); (2) consistent results, with minor and/or few exceptions; (3) minor and/or few concerns about study quality; and/or (4) the extent of Expert Panelists' agreement. Other compelling considerations (discussed in the guideline's literature review and analyses) may also warrant a moderate recommendation.
Weak	There is some confidence that the recommendation offers the best current guidance for practice. This is based on (1) limited evidence for a true net effect (e.g., benefits exceed harms); (2) consistent results, but with important exceptions; (3) concerns about study quality; and/or (4) the extent of Expert Panelists' agreement. Other considerations (discussed in the guideline's literature review and analyses) may also warrant a weak recommendation.

Cost Analysis

The guideline developer reviewed a published cost analysis.

Method of Guideline Validation

External Peer Review

Internal Peer Review

Description of Method of Guideline Validation

Members of the Expert Panel were responsible for reviewing and approving the penultimate version of guideline, which was then circulated for external review and submitted to *Journal of Clinical Oncology* for editorial review and consideration for publication. All American Society of Clinical Oncology (ASCO) guidelines are ultimately reviewed and approved by the Expert Panel and the ASCO Clinical Practice Guideline Committee (CPGC) before publication.

External Review

The draft was submitted to two external reviewers with content expertise. Based on the reviews, revisions were made by co-chairs and shared with the Expert Panel for approval.

The CPGC approved this guideline on April 10, 2017.

Evidence Supporting the Recommendations

Type of Evidence Supporting the Recommendations

The type of supporting evidence is identified and graded for each recommendation (see the "Major Recommendations" field).

Benefits/Harms of Implementing the Guideline Recommendations

Potential Benefits

Adherence to antiemetic guidelines has been linked to improved control of nausea and vomiting.

Refer to the "Literature review update and analysis" and "Clinical interpretation" sections of the original guideline document for a detailed discussion of the potential benefits of each recommendation.

Potential Harms

Adverse events associated with use of antiemetics, including neutropenia, insomnia, heartburn, headache, constipation, diarrhea, dizziness, anemia, and drowsiness.

Refer to the "Literature review update and analysis" and "Clinical interpretation" sections of the original guideline document for a detailed discussion of the potential harms of each recommendation. See also Table 2 in the Data Supplement (see the "Availability of Companion Documents" field) for specific adverse events.

Qualifying Statements

Qualifying Statements

- Although this guideline provides estimates of the emetic risk of both intravenous (IV) and oral antineoplastic agents, emetic risk information is limited and variable for many of the oral agents. As a result, the recommendations in this guideline for antineoplastic-related nausea and vomiting are most definitive for adults who are treated with single-day intravenous (IV) chemotherapy.
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- See the "Health Disparities" section in the original guideline document for additional qualifying information.

Implementation of the Guideline

Description of Implementation Strategy

For information on the American Society for Clinical Oncology (ASCO) implementation strategy, please see the ASCO Web site .

Implementation Tools

Mobile Device Resources

Patient Resources

Quick Reference Guides/Physician Guides

Resources

Slide Presentation

For information about availability, see the *Availability of Companion Documents* and *Patient Resources* fields below.

Institute of Medicine (IOM) National Healthcare Quality Report Categories

IOM Care Need

Getting Better

Living with Illness

IOM Domain

Effectiveness

Patient-centeredness

Identifying Information and Availability

Bibliographic Source(s)

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Adaptation

Not applicable: The guideline was not adapted from another source.

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Guideline Committee

Antiemetics: American Society of Clinical Oncology Clinical Practice Guideline Update Expert Panel

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Financial Disclosures/Conflicts of Interest

Guideline and Conflicts of Interest

The Expert Panel was assembled in accordance with the American Society of Clinical Oncology's (ASCO's) Conflict of Interest Policy Implementation for Clinical Practice Guidelines ("Policy," found at www.asco.org/about-asco/legal/conflict-interest). All members of the Expert Panel completed ASCO's disclosure form, which requires disclosure of financial and other interests, including relationships with commercial entities that are reasonably likely to experience direct regulatory or commercial impact as a result of promulgation of the guideline. Categories for disclosure include employment; leadership; stock or other ownership; honoraria; consulting or advisory role; speakers' bureau; research funding; patents, royalties, other intellectual property; expert testimony; travel, accommodations, expenses; and other relationships. In accordance with the Policy, the majority of the members of the Expert Panel did not disclose any relationships constituting a conflict under the Policy.

Authors' Disclosures and Potential Conflicts of Interest

The following represents disclosure information provided by authors of the guideline. All relationships are

considered compensated. Relationships are self-held unless noted. I = Immediate Family Member, Inst = My Institution. Relationships may not relate to the subject matter of this manuscript. For more information about ASCO's conflict of interest policy, please refer to www.asco.org/about-asco/legal/conflict-interest or ascopubs.org/jco/site/ifc.

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Guideline Status

This is the current release of the guideline.

This guideline updates a previous version: Basch E, Prestrud AA, Hesketh PJ, Kris MG, Feyer PC, Somerfield MR, Chesney M, Clark-Snow RA, Flaherty AM, Freundlich B, Morrow G, Rao KV, Schwartz RN, Lyman GH. Antiemetics: American Society of Clinical Oncology clinical practice guideline update. J Clin Oncol. 2011 Nov 1;29(31):4189-98. [56 references]

This guideline meets NGC's 2013 (revised) inclusion criteria.

Guideline Availability

Available from the Journal of Clinical Oncology Web site .

This guideline is also available in the ASCO guidelines app .

Availability of Companion Documents

The following are available:

Antiemetics: American Society of Clinical Oncology clinical practice guideline update summary. J Oncol Pract. 2017 Dec;13(12):825-30. Available to subscribers from the Journal of Oncology Practice Web site .

Antiemetics: American Society of Clinical Oncology clinical practice guideline update. Data supplements. Alexandria (VA): American Society of Clinical Oncology; 2017. 78 p. Available from the Journal of Clinical Oncology Web site .

Antiemetics: American Society of Clinical Oncology clinical practice guideline update. Methodology supplement. Alexandria (VA): American Society of Clinical Oncology; 2017. 18 p. Available from the Journal of Clinical Oncology Web site .

Antiemetics: American Society of Clinical Oncology clinical practice guideline update. Slide set. Alexandria (VA): American Society of Clinical Oncology; 2017. 33 p. Available in PDF and PowerPoint from the ASCO Web site.

ASCO 2017 antiemetics guideline update: drug, dose, schedule recommendations for antiemetic regimens. Alexandria (VA): American Society of Clinical Oncology; 2017. 6 p. Available from the ASCO Web site .

Emetic risk of single intravenous antineoplastic agents in adults. Alexandria (VA): American Society of Clinical Oncology; 2017. 1 p. Available from the ASCO Web site .

Emetic risk of single oral antineoplastic agents in adults. Alexandria (VA): American Society of Clinical Oncology; 2017. 1 p. Available from the ASCO Web site .

Emetic risk in adults by site of radiation therapy. Alexandria (VA): American Society of Clinical Oncology; 2017. 1 p. Available from the ASCO Web site .

Patient Resources

The following is available:

Nausea and vomiting. Patient information. [internet]. Alexandria (VA): American Society of Clinical Oncology (ASCO); 2017 Jul. Available from the Cancer.Net Web site .

Please note: This patient information is intended to provide health professionals with information to share with their patients to help them better understand their health and their diagnosed disorders. By providing access to this patient information, it is not the intention of NGC to provide specific medical advice for particular patients. Rather we urge patients and their representatives to review this material and then to consult with a licensed health professional for evaluation of treatment options suitable for them as well as for diagnosis and answers to their personal medical questions. This patient information has been derived and prepared from a guideline for health care professionals included on NGC by the authors or publishers of that original guideline. The patient information is not reviewed by NGC to establish whether or not it accurately reflects the original guideline's content.

NGC Status

This summary was completed by ECRI on January 3, 2000. It was verified by the guideline developer on January 18, 2000. This NGC summary was updated by ECRI on July 25, 2006. This summary was updated by ECRI Institute on April 1, 2009 following the FDA advisory on Reglan (metoclopramide). This summary was updated by ECRI Institute on May 1, 2009 following the U.S. Food and Drug Administration advisory on antiepileptic drugs. This summary was updated by ECRI Institute on January 12, 2011 following the U.S. Food and Drug Administration advisory on Anzemet (dolasetron mesylate). This NGC summary was updated by ECRI Institute on December 8, 2011. This summary was updated by ECRI Institute on

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